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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/501,496	07/14/2004	John R. Fozard	PA/4-32352A	8265

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EXAMINER

CHONG, YONG SOO

ART UNIT	PAPER NUMBER
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1617

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/13/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No. 10/501,496	Applicant(s) FOZARD ET AL.	
	Examiner Yong S. Chong	Art Unit 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 February 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 10-29 is/are pending in the application.
 4a) Of the above claim(s) 20 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 10-19 and 21-29 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the Application

This Office Action is in response to applicant's arguments filed on 2/20/2007. Claim(s) 1-9 have been cancelled. Claim(s) 10-29 are pending. Claim(s) 11-19, 21-28 have been amended. Claim(s) 20 has been withdrawn. Claim(s) 10-19, 21-29 are examined herein.

Applicant's amendments to the claims have rendered the 112 rejection of the last Office Action moot, therefore hereby withdrawn.

Applicant's arguments have been fully considered but found not persuasive. The rejection(s) of the last Office Action are maintained for reasons of record and repeated below for Applicant's convenience.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim(s) 10-19, 21, 27-29 are rejected under 35 U.S.C. 102(b) as being anticipated by Gerspacher et al. (WO 98/07694).

Gerspacher et al. disclose acylaminoalkenylene-amide derivatives of formula I (abstract) for the treatment of gastrointestinal disorders such as Crohn's disease, ulcerative colitis, and diarrhea (pg. 5, paragraphs 1-2). A preferred compound is

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disclosed to be (4R)-4-[N'-methyl-N'-(3,5-bis(trifluoromethyl)-benzoyl)-amino]-4-(3,4-dichlorobenzyl)-but-2-enoic acid N-[(R)-epsilon-caprolactam-3-yl]-amide (pg. 33, paragraph 3) to be administered to a warm-blooded animal from approximately 1 to 1000 mg (pg. 16, paragraph 3).

Response to Arguments

Applicant argues that the diseases of the gastrointestinal tract, Crohn's disease, ulcerative colitis, and diarrhea, as disclosed by Gerspacher et al. are not functional motility disorders of the viscera of the instant invention.

This is found not persuasive because the very definition of functional motility disorders of the viscera as disclosed in Applicant's disclosure include functional bowel disorders, functional gastrointestinal disorders, IBS, constipation, diarrhea, abdominal pain and bloating (pg. 2, first paragraph). Moreover, Applicant has explicitly stated, "treatment of a functional motility disorder of the viscera in accordance to this invention may be symptomatic or prophylactic (preventative)." Therefore, according to the Applicant, the patient population of this invention does not have to show symptoms of functional motility disorders of the viscera.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham vs John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim(s) 22-26 are rejected under 35 U.S.C. 103(a) as being obvious over Gerspacher et al. (WO 98/07694) as applied to claims 10-19, 21, 27-29 in view of Ksander et al. (US Patent 5,217,996).

The instant claims are directed to a method of treating diarrhea-predominant irritable bowel syndrome by administering (4R)-4-[N'-methyl-N'-(3,5-bistrifluoromethyl-benzoyl)-amino]-4-(3,4-dichlorobenzyl)-but-2-enoic acid N-[(R)-epsilon-caprolactam-3-yl]-amide.

Gerspacher et al. teach as discussed above, however, does not specifically disclose diarrhea-predominant irritable bowel syndrome.

Ksander et al. disclose a general teaching that some examples of gastrointestinal disorders are diarrhea and irritable bowel syndrome (col. 1, lines 35-37).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed invention was made, to have used (4R)-4-[N'-methyl-N'-(3,5-bistrifluoromethyl-benzoyl)-amino]-4-(3,4-dichlorobenzyl)-but-2-enoic acid N-[(R)-epsilon-caprolactam-3-yl]-amide, as disclosed by Gerspacher, to treat diarrhea-predominant irritable bowel syndrome.

A person of ordinary skill in the art would have been motivated to treat diarrhea-predominant irritable bowel syndrome because (1) Gerspacher et al. teach a method of treating gastrointestinal disorders such as diarrhea and (2) Ksander et al. teach that both diarrhea and irritable bowel syndrome are examples of gastrointestinal disorders. Therefore, one of ordinary skill in the art would have had a reasonable expectation of success in treating diarrhea-predominant irritable bowel syndrome with (4R)-4-[N'-methyl-N'-(3,5-bistrifluoromethyl-benzoyl)-amino]-4-(3,4-dichlorobenzyl)-but-2-enoic acid N-[(R)-epsilon-caprolactam-3-yl]-amide.

Examiner notes that this is a typical genus/species situation. Once a *prima facie* case of obviousness is established, the burden is shifted to the Applicant for objective evidence for nonobviousness. See MPEP 2144.08.

Response to Arguments

Applicant argues that Ksander does not disclose acylaminoalkenylene-amide derivatives of formula I of the claimed invention.

In response to applicant's arguments against the references, one cannot show nonobviousness by attacking references individually where the rejections are based on the combination of references. See *In re Keller*, 642 F. 2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F. 2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant also argues that Ksander merely mentions irritable bowel syndrome and diarrhea as potential indications in the summary of invention, and that this is purely speculative. No support is given for this assertion other than biaryl substituted 4-amino-butyric acid amides are apparently NEP inhibitors.

This is found not persuasive because Ksander was merely used for the general teaching that some examples of gastrointestinal disorders are diarrhea and irritable bowel syndrome. The fact that Ksander has or doesn't have support is irrelevant to this obviousness rejection.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong S. Chong whose telephone number is (571)-272-8513. The examiner can normally be reached on M-F, 9-6.

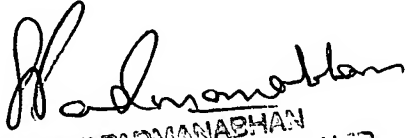
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, SREENI PADMANABHAN can be reached on (571)-272-0629. The fax

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phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

YSC


SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER